**Remarks**

**Formal Matters**

Claims 6-22 are pending after entry of the amendments set forth herein.

Claims 18-22 have been withdrawn from consideration.

Claims 6-10 have been amended. Support for the amendments can be found in claims as originally filed and throughout the specification at, for example: Claim 6: original Claims 1 and 8; Claim 7: page 2, last paragraph; page 37, lines 15-21; Claim 8: page 20, lines 4-15. Claims 9 and 10 have been amended to correct typographical errors.

The specification has also been amended on page 20 in order to correct a typographical error.

As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

**Objections**

***Claim 6***

Claim 6 has been objected to for depending from a canceled claim. Claim 6 has been amended to incorporate the limitations of Claim 1. As such, in view of the amendment to the claim, this objection is rendered moot.

***Claim 10 and the Specification***

Claim 10 and the specification have been objected to for using the designation "SEQ ID No." rather than the designation "SEQ ID No:". In particular the Examiner notes that the speciation on pages 16 and 26 should be amended to correct the improper designation. The Applicants note that there is no use of such a designation on the pages noted by Examiner. However, the improper designation was found on page 20 and has been amended to correct the typographical error. As such in view of the amendments to Claim 10 and page 20 of the specification, this objection is rendered moot.

**Rejection under 35 U.S.C. §112, first paragraph**

Claims 6-17 have been rejected under 35 U.S.C. § 112, first paragraph, on the grounds that the specification allegedly failes to enable the claimed invention. In particular, the Office Action asserts that the specification only provides enablement for a fusion protein comprising GFP or EGFP and $MDOC_{376-461}$, $MDOC_{376-456}$, or $MDOC_{422-461}$. As the Applicants understand it, the rejection is based on the assertion that the specification does not provide enablement for any fusion protein having a half-life of no more than about 10 hours (Office Action, page 4). This rejection is respectfully traversed.

Without conceding to the correctness of the rejection and in the spirit of expediting prosecution, Claim 6 has been amended to recite an isolated DNA molecule encoding a fusion protein "**said fusion protein comprising a fluorescent protein and a PEST sequence**".

The law is clear that "[t]he test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." United States v. Telectronics, Inc., 8 USPQ 2d 1217, 1233 (Fed. Cir. 1988), cert. denied, 490 U.S. 1046 (1989). See also, Genentech, Inc. v. Novo Nordisk, 42 USPQ 2d 1001 (Fed. Cir. 1997), cert. denied, 522 U.S. 963 (1997); Scripps Clinic and Research Foundation v. Genentech, Inc., 18 USPQ 2d 1001 (Fed. Cir. 1991).

Furthermore, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. In re Certain Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia, 227 USPQ 428 (Fed. Cir. 1985). See also, MPEP §2164.01. Practitioners in the chemical and molecular biology arts frequently engage in extensive modification of reaction conditions and complex and lengthy experimentation where many factors must be varied to succeed in performing an experiment or in producing a desired result. The Federal Circuit has found that such extensive experimentation is not undue in the molecular biology arts. For example, in Hybritech v. Monoclonal Antibodies, Inc. (231 USPQ 81 (Fed. Cir. 1986)) the court concluded that extensive screening experiments, while being

voluminous, were not undue in view of the art which routinely performs such long experiments.

The experimentation in the instant invention was directed toward determining whether adding a PEST sequence from a short lived protein would cause a fluorescent protein to be shorter lived. The PEST sequence from amino acids 422-461 of murine ornithine decarboxylase (MODC) and variants thereof were determined to effectively shorten the life of a fluorescent protein. The results show that adding a PEST sequence to a fluorescent protein was effective in shortening the life of the protein. As there is no reason to believe that all PEST sequences do not shorten protein lifespans by the same mechanism, one skilled in the art would thus expect addition of any other PEST sequence to result in similar results. The specification at, for example, page 20 provides detailed information regarding a variety of other PEST sequences that are suitable for use with the claimed invention.

The specification provides several working examples for a variety of fluorescent proteins that are suitable for use with the claimed invention. For example, the specification provides working examples using GFP and EGFP, as noted in the Office Action, as well as ECFP and EYFP (see Example 9). Since fluorescent proteins are well known in the art, one skilled in the art would thus expect other fluorescent proteins to provide similar results.

Compliance with the enablement requirement under 35 U.S.C. §112, first paragraph does not require or mandate that a specific example be disclosed. The specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art would be able to practice the invention without undue experimentation.[1] Furthermore, "[n]othing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples."[2]

Accordingly, based on the guidance provided in the specification of the present application and the relevant art, it would be reasonable to conclude that other fluorescent proteins are suitable for use with the claimed invention other than GFP and

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[1]. *In re Borkowski,* 164 U.S.P.Q. 642, 645 (CCPA 1970).
[2]. *In re Robins* 166 U.S.P.Q. 552, 555 (CCPA 1970).

EGFP, which were exemplified in Example 5, or ECP and EYFP, which were exemplified in Example 9.

Therefore one skilled in the art would expect that since the instant invention demonstrated that $MODC_{422-461}$, $MODC_{376-451}$, and $MODC_{376-456}$ are capable of effectively shortening the lifespan of fluorescent proteins, such as GFP, EGFP, ECFP, and EYFP, any PEST sequence from proteins other than MODC would have the same effect on other fluorescent proteins. Accordingly, the present specification provides an enabling disclosure to practice the claimed invention.

As such, the Applicants submit that the rejection of Claims 6-17 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the amendments to the claims as well as the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

**Rejection under 35 U.S.C. §112, second paragraph**

***Claim 7***

Claim 7 has been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. The Examiner asserts that Claim 7 is allegedly indefinite for the use of abbreviations without using the full name. In view of the amendment to the claim this rejection is rendered moot.

***Claims 8 and 9***

Claims 8 and 9 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. In particular, the Examiner notes that the use of the abbreviation "PEST" is indefinite. The Applicants note that the term PEST is the term used to refer to a sequence that is rich in proline (P), glutamic acid (E), serine (S), and threonine (T) residues (see, for example, specification, page 3). The term is not specifically a direct abbreviation of a full term. Accordingly, the applicants respectfully request that this rejection be withdrawn.

**Rejection under 35 U.S.C. §102(b)**

Claims 6, 11-17 have been rejected under 35 U.S.C. § 102(b) as allegedly being

anticipated by Moradpour et al. (Virology, 222:51-63, 1993). This rejection is respectfully traversed.

Moradpour et al. discloses a fusion protein comprising a Hepatitis C Viral core protein fused to luciferase, wherein the fusion protein has an intracellular half-life of 9 hours.

Without conceding to the correctness of the rejection and in the sprit of expediting prosecution, Claim 6 has been amended to recite "DNA molecule encoding a fusion protein comprising a fluorescent protein and **a PEST sequence**, said fusion protein having a half life of no more than about ten hours."

Moradpour et al. fails to disclose a fusion protein comprising a fluorescent protein and a **PEST sequence**. As such, since the cited reference fails to teach each and every limitation of the present invention, the cited reference fails to anticipate Claims 6, 11-17. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

**Conclusion**

Applicant submits that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815.

Respectfully submitted,
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Date: September 23, 2004

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